REMARKS

Claim 14 was pending in the subject application. In this Amendment claim 14 has been amended. Claim 14 is still pending in the subject application.

Claim 14 has been amended to specify that "said composition is administered in an amount sufficient to promote the secretion of antiviral factors in the respiratory tract." Support for the amendment to claim 14 can be found in the original specification at, for example, page 11, lines 15-16.

No new matter is added by this amendment, and Applicants respectfully request its entry.

I. Rejection of Claim 14 under 35 U.S.C. § 112, first paragraph

The Examiner rejected claim 14 under 35 U.S.C. § 112, first paragraph as allegedly being non-enabling for the reasons set forth in the office action. In particular, the Examiner focuses on four of the eight factors set forth in *In re Wands* and contends that those skilled in the art could not make and use the full scope of the invention without undue experimentation. The Examiner bases his rejection on the same grounds as those set forth in the office action mailed on June 5, 2008 which are discussed below:

(A) The nature of the invention, state and predictability of the art, and relative skill to those in the art

The Examiner refers to Yang et al., Eur. Respir. J. 2002, 19:952-958 ("Yang et al."); Harper et al., Prevention and Control of Influenza, May 28, 2004 53 (RR-6):1-40 ("Harper et al."); and WO 95/07103 to Mitra et al. ("Mitra et al.") "[a]s illustrative of the state of the art." The Examiner asserts that the "references plainly demonstrate that prevention of influenza is an art recognized hurdle. The references also demonstrate that influenza can be treated, proliferation can be suppressed, and the incidence thereof can be reduced." The Examiner states, however, that "there is nothing in the art that supports prevention of infection of the flu virus." Applicants disagree.

In the Amendment filed on October 16, 2008 ("the October 16, 2008 Amendment") (the entire content of which is incorporated herein by reference), Applicants discussed each of the references and noted that nothing in any of the cited references indicated that ambroxol cannot be used to prevent infection of the flu virus as asserted by the Examiner. In the present office action, the Examiner "agrees that Yang, Harper and Mitra do not expressly

state that ambroxol cannot be used to prevent infection of the flu virus. However, they do not expressly state that it can be used to prevent infection of the flu either."

In the October 16, 2008 Amendment, Applicants also argued that the state of the art at the time the subject invention was filed supports the use of ambroxol to prevent infection of the flu virus. For example, Applicants argued that the subject specification states that ambroxol and/or bromhexin has an anti-oxidative effect and can serve as a sputum-dissolving agent capable of promoting the release of pulmonary surfactants (PS) (see page 4, line 26 to page 5, line 1). Applicants also noted that the specification of the subject application described pulmonary surfactants in the lung as part of the "principal immunological defensive system for preventing any invasion of viruses into cells and more specifically, the induction of local secretion of immunoglobulin Iga and IgG is closely related to the protection from the influenza virus infection (Refs. 11-13)" (see page 2, lines 16-26). Applicants also noted that the specification describes "ambroxol [as having] such pharmacological functions as the control of mucus on the adenocyte of the respiratory tract and the promotion of the PS-production (Ref. 15)" (see page 3, lines 24-26). Based on the above, Applicants argued (and continue to maintain) that claim 14 of the subject application which recites "a method for preventing an influenza virus infection in a warm-blooded animal, which comprises administering to such animal a therapeutically effective amount of a composition comprising an agent selected from ambroxol, bromhexin, the pharmaceutically acceptable salts of ambroxol or bromhexine and combinations thereof, and an additive" was predictable.

Applicants also note the contradictory positions taken by the Examiner in the present office action where the Examiner argues that Mitra does not "support[] prevention of infection of the flu virus" (i.e., Mitra does not teach enablement) while also arguing that Mitra anticipates the claimed invention (which requires that Mitra is enabling). (See Section II below.) Applicants note in particular the Examiner's statement that "prevention of an influenza virus' is inherent to Mitra[]."

Since Mitra is enabled (as asserted by the Examiner and discussed in Section II below), then Mitra also supports prevention of infection of the flu virus.

(2) <u>The breadth of the claims</u>

With regard to the breadth of the claims, the Examiner states that "[i]nfection is defined in the art as the process by which a viral particle (i.e., a virion) enters (i.e., injects) a host cell. See Figures 6-15 and 6-16 at pages 195 and 196 of *Molecular Cell Biology*.

Prevention as claimed in its broadest most reasonable interpretation means a virion never injects into a single host cell." However, it is not clear to Applicants why this reference is relevant to the breadth of claim 14. For the reasons already discussed in the October 16, 2008 Amendment, the method recited in claim 14 is disclosed in the specification and is within the skill of those in the art for the reasons discussed in Section (1) above which is in accord with requirements set forth in MPEP § 2164.08 ("As concerns the breadth of a claim relative to enablement, the only relevant concern should be whether the scope of the enablement provided to one skilled in the art by the disclosure is commensurate with the scope of the protection sought by the claims.").

(3) The amount of direction or guidance provided and the presence or absence of working examples

With regard to the direction or guidance, the Examiner again states that "[t]he specification provides no direction for determining the particular administration regimes (dosage, timing, administration routes, etc.) necessary to prevent an influenza virus infection in warm-blooded animals." With regard to working examples, the Examiner states that "[t]he working examples are limited to treating and inhibiting proliferation of the influenza virus. Thus, the applicant at best has provided specific direction or guidance only for treating and inhibiting proliferation of an influenza virus infection." The Examiner contends that "[no reasonably specific guidance is provided concerning useful preventive protocols for an influenza infection." Applicants disagree.

As discussed in the October 16, 2008 Amendment, it was known in the art at the time of filing the subject application that ambroxol could be used to prevent chronic bronchitis based in part on the production of pulmonary surfactants. Applicants also noted that the ambroxol increases the production of pulmonary surfactants, and pulmonary surfactants are the "principal immunological defensive system for preventing any invasion of viruses into cells." In the present office action, the Examiner states that the above statement was made in regards to the reference to Benne et al.," *J. Infect. Dis.*, 171: 335-341 (1995) ("Benne") in the specification. The Examiner indicated the Benne reference must be submitted on form PTO-892 as part of an information disclosure statement (IDS) in order to be considered.

Filed concurrently herewith is an IDS which includes a copy of the Benne reference for consideration by the Examiner. Benne relates to the interaction of pulmonary surfactant protein A (SP-A) with influenza H1H1 and H3N2 viruses. According to Benne, "SP-A binds

to influenza A viruses via its sialic acid residues and, thereby, neutralizes the virus" (see Abstract of Benne).

In summary, SP-A can neutralize flu viruses (e.g., influenza H1H1 and H3N2) as described by Benne. And ambroxol increases the production of pulmonary surfactants (e.g., SP-A) as described in the subject application. Thus, administering to a warm-blooded animal a therapeutically effective amount of a composition comprising ambroxol and/or bromhexin, would lead to increased SP-A production in the animal, a higher likelihood of neutralizing the influenza virus, and, therefore, a higher likelihood that the animal would not be infected by the influenza virus. Therefore, one of skill in the art would have sufficient guidance to use ambroxol to prevent in influenza virus infection without undue experimentation.

(4) The quantity of experimentation necessary

With regard to the quantity of experimentation, the Examiner refers to the art-recognized hurdle discussed above and again asserts that "in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed method could be predictably used to prevent an influenza virus infection as inferred in the claims and contemplated by the specification."

Applicants disagree. For the reasons discussed in Sections (1) - (3) above and in the October 16, 2008 Amendment, a skilled artisan would appreciate that claim 14 is commensurate in scope with the specification, and claim 14 could be practiced without undue experimentation.

In view of the above, Applicants respectfully submit that claim 14 is enabled, and request that the rejection of claim 14 under 35 U.S.C. § 112, paragraph 1 be withdrawn.

II. Rejection of Claim 14 under 35 U.S.C. § 102(b)

The Examiner rejected claim 14 under 35 U.S.C. 102(b) as allegedly being anticipated by Mitra for the reasons set forth in the office action. In particular, the Examiner states that "Mitra teaches the compositions and methods for providing improved treatment, management or mitigation of cold, cold-like and/or flu symptoms in a mammal by administering a safe and effective amount of a composition comprising an amino acid salt of propionic acid nonsteroidal anti-inflammatory agent (i.e., and additive) along with at least one of (a) a decongestant, (b) an expectorant, (c) and antihistamine and (d) and antitussive

(see Abstract and claims 1 and 8)." The Examiner further states that "Mitra also names the specific expectorants , 'bromhexine and ambroxol, mixtures thereof or pharmaceutically acceptable salts thereof' (see claim 3)." The Examiner still further states that "Mitra does not explicitly state the particular limitation 'for preventing an influenza virus infection' found in instant method claim 14, however Mitra teaches treating, management or mitigation of flu symptoms in a mammal comprising the same ingredients." The Examiner asserts that "'prevention of an influenza virus' is inherent to Mitra's 'treatment, management or mitigation of cold, cold-like and/or flu symptoms' because the method of Mitra and the claimed method include the same method steps and are treating the same patient population. Thus, Mitra implicitly teaches the claimed method." Applicants traverse.

As a threshold matter, Applicants note again the contradictory positions taken by the Examiner in the present office action where the Examiner argues that Mitra does not "support[] prevention of infection of the flu virus" (i.e., Mitra is not enabling for prevention) while simultaneously arguing that Mitra anticipates the claimed invention (which requires that Mitra is enabling for prevention). (See Section I above.)

"To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate." *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education and Research*, 346 F.3d 1051, 1055 (Fed. Cir. 2003). "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003).

Even if Mitra is an enabling reference, Applicants submit that Mitra does not anticipate claim 14 of the subject application.

Amended claim 1 of the subject application recites "a method for preventing an influenza virus infection in a warm-blooded animal, which comprises administering to such animal an effective amount of a composition comprising an agent selected from ambroxol, bromhexin, the pharmaceutically acceptable salts of ambroxol or bromhexine and combinations thereof, and an additive" and further specifies that "said composition is administered in an amount sufficient to promote the secretion of antiviral factors in the respiratory tract." Such aspect of claim 14 is not described or even suggested in Mitra.

Mitra discloses a composition comprising a derivative of a non-steroidal anti-inflammatory agent along with "at least one of a (a) a decongestant, (b) an expectorant (c) an antihistamine and (d) an antitussive" (see page 1, lines 8-10 of Mitra). Mitra also lists

examples of decongestants, expectorants, antihistamines and antitussives (see page 5, lines 13-32; and page 12, claim 3). The Examine refers to claim 3 of Mitra which recites about 46 decongestants, expectorants, antihistamines and antitussives. Included in this list of 46 additional agents is bromhexin and ambroxol, which Mitra describes as "expectorants." However, nowhere does Mitra disclose a composition comprising any expectorant, let alone a composition comprising bromhexin and/or ambroxol. Moreover, even if one of skill in the art would select bromhexin and/or ambroxol, nothing in Mitra describes using the bromhexin and/or ambroxol (or a composition comprising bromhexin and/or ambroxol) "in an amount sufficient to promote the secretion of antiviral factors in the respiratory tract" as recited in amended claim 14.

In order to anticipate a claim, "[t]he identical invention must be shown in as complete detail as is contained in the … claims." MPEP § 2131 (quoting Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236 (Fed Cir. 1989)).

Mitra does not show the identical invention as recited in amended claim 14 of the subject application. Therefore, Mitra does not anticipate amended claim 14.

In view of the above, Applicants request that the rejection of claim 14 under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

Applicants respectfully request prompt consideration of the pending claims and early allowance of the application. No additional fee is believed due. However, if any additional fee is due, the Examiner is authorized to charge the fee to Applicants' Deposit Account No. 02-2955.

If a telephonic or personal interview is deemed necessary to expedite the examination of the instant application, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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Date: April 30, 2009